DETAILED ACTION

Acknowledgement is made of the remarks and amendments filed 5/19/2009. Claims 1-8 and 16 stand canceled. Claims 17 and 20 were amended. Claims 17-24 remain withdrawn for being directed to a non-elected invention. Claims 9-15 and 17-25 are pending and claims 9-15 and 25 are under consideration in the instant Office action.

Withdrawn Claim Rejections

Claim Rejections - 35 USC § 103

The rejection of claims 9-10 under 35 U.S.C. 103(a) as being unpatentable over Lopresti et al. (LoPresti. Characteristics of 3,5,3'-Triiodothyronine Sulfate Metabolism in Euthyroid Man. Journal of Clinical Endocrinology and Metabolism, Vol. 73, No. 4, 1992, pages 703-709; already made of record), in view of Miura et al. (US Patent 5,116,828; already made of record) is withdrawn due to the fact that 25 microCuries of ^{125}I labeled T3S equates to a smaller amount than is required by the instant claims (5-1000 micrograms). It is noted, however, that applicant notes that Lopresti discloses that ^{125}I labeled T3S has an activity ranging from 1000-2000mCi/mg. The Examiner read the disclosure of Lopresti in detail and cannot find this teaching. However, this conversion-teaching aside, it is the position of the Examiner that one of ordinary skill in the art would never administer as large of a dosing as called for by the claims of a radioactive compound for risk of killing the patient, therefore Lopresti fails to render the claims obvious. Therefore the rejection is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-15 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Santini et al. Thyromimetic effects of 3,5,-3'-triiodothyronine sulfate in hypothyroid

rats. Endocrinology. 1993;133(1): 105-110; already made of record by applicant), in view of Miura et al. (US Patent 5,116,828; already made of record).

Santini et al. (Santini et al. Thyromimetic effects of 3,5,-3'-triiodothyronine sulfate in hypothyroid rats. Endocrinology. 1993;133(1): 105-110; already made of record by applicant) teach that treatment of hypothyroid thyroidectomized (Tx) rats with T3S and T3 in doses of 0.46 and 2.3 nmol/day for 10 days via intraperitoneal (i.p.) injection results in marked improvement in the growth of the treated rats (abstract). Santini et al. concluded that administration of T3S to hypothyroid rats produces thyromimetic effects with a potency one fifth that of T3 (abstract). Santini et al. also teach that sulfatases have been found in tissues and the intestinal flora that convert T3S back to the parent hormone (T3) and therefore T3S might represent a reserve pool of T3 to attenuate the effects of reduced generation of T3 from T4 (thyroxine) under conditions where monodeiodinase (MD) activity is reduced e.g. fetal life, fasting, nonthyroidal illnesses, hypothryroidism, and selenium deficiency even though the exact amount of T3 that could be generated by desulfation of T3S is not known (page 105, col. 1, second para., lines 5-12). Santini et al. et al. further suggest that T3S may reduce the risk of inducing hyperthyroidism when compared to T4 and that more studies are necessary to test this possibility (page 109, first para., last three lines to last para., last line).

It is unclear if Santini et al dosage falls within applicant's instantly claimed amount of T3S as recited in claims 9-10. It is requested that applicant provide the conversion of nMol to µg of TS3.

Although Santini et al. teach formulations comprising T3S, this reference does not teach compositions comprising T3S in the specific instantly claimed amount of 5 to 1000 µg. Further, Satini et al. do not teach the instant claimed combination of T3S and thyroxine.

Miura et al teach L-thyroxine (T4) in doses of 25-400 µg/day, and L-triiodothyronine (T3) in doses of 5-150 µg/day (see col. 3, lines 1-4).

It would have been obvious to a person of skill in the art at the time the invention was made to manipulate the dosage amount of T3S in the composition taught by Santini et al., including applicant's claimed dosage amount of 5 to 1000 µg., based on patient parameters such as age, weight, and severity of condition. Besides, Santini et al. teach that T3S produces thyromimetic effects one fifth that of T3 (abstract). To the extent that Miura et al. teach L-triiodotyronine (T3) in doses of 5-150 µg/day, one would reasonably expect to administer T3S in an equivalent dosage amount of five times the T3 dose taught by Miura et al.(or 25 – 750 µg T3S) to treat hypothyroidism, which overlaps with the instant claimed dosage range of T3S (claims 9-10).

Further, it would have been obvious to a person of skill in the art at the time the invention was made to add thyroxine (T4) in a dosage range of 25-400 µg as taught by Miura et al. to the T3S composition as taught by Santini et al. for additive effects in treating hypothyroidism. One would have been motivated to do so because T3S as taught by Santini et al. and T4 as taught by Miura et al. are thyromimetic agents (see In re Kerkhoven, 205 USPQ 1069 (CCPPA 1980).

It is noted that the dosage range of 25-400 µg thyroxine taught by Miura et al. overlaps with the instant claimed thyroxine dosage range recited in claims 11, 13, 15, and 25.

With respect to claims 14, 15 and 25 which are directed to a kit, it is the examiner's position that it would have been obvious to a person of skill in the art at the time the invention was made to supply T3S and thyroxine the same package (= kit) for patient convenience. One would have been motivated to do so because by packaging T3S and thyroxine in the same package (= kit) would improve patient compliance because this would reduce the chances of a patient forgetting to take both agents.

Thus, it would have been obvious to a person of skill in the art at the time the invention was made to create the instant claimed invention with reasonable predictability.

Response to arguments

It is noted that no new rejections have been presented in this Office action. Previously the teachings of Miura were found in the rejection of claims over Lopresti et al. in view of Miura et al. (now withdrawn), accordingly the Examiner has directly incorporated these exact same teachings into the above rejection of claims over Santini et al. in view of Miura et al.

Applicant's arguments filed 5/16/2009 in response to the rejection of claims have been fully considered, but are not persuasive.

Applicant argues that a prima facie case of obviousness has not been established. More specifically, applicant argues that Santini is directed exclusively to

the intraperitoneal injection of T3S and the thyromimetic acitivity discussed resulted only from such intraperitoneal administration. Applicant argues that neither does Santini teach nor suggest oral administration and that Miura fails to remedy this deficiency. This argument is not persuasive for the following reasons.

In response to applicant's argument that the teachings of Santini and Miura do not teach oral administration, a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. Here, the phrase "for oral administration" in the claims is the future intended use of the claim. Because the composition as taught by Santini in further view of Miura contains no substance which would inhibit its use orally (i.e. nothing toxic), as evidenced by the fact that intraperitoneal administration is non-toxic and non-lethal, the teachings render the claimed composition obvious.

As an aside, it is noted additionally, that Santini alone teaches a composition having 11.5 nmol of T3S (abstract). Assuming a molecular weight of T3S of roughly 745 g/mol, this equates to roughly 8.6 micrograms per day and anticipates claim 9. Anticipation is the perfect example of a prima facie case of obviousness.

Applicant also argues that Lopresti (the primary references in the rejection that is now withdrawn), teaches that T3S is an inactive metabolite which was not absorbed by the GI system upon oral administration. Therefore applicant concludes that one skilled in the art would have no expectation that T3S would be properly absorbed upon oral

ingestion so as to act as an oral thyromimetic drug. Again, this argument is not persuasive because it is based solely on the intended use of the composition. Furthermore, as addressed above in the withdrawal of the rejection of claims over Lopresti in view of Miura, the amount of radioactive ^{125}I-T3S is far smaller than the amount required by the instant claims. One of ordinary skill in the art would not expect a lesser amount to have any effect, which is what is observed in Lopresti.

Applicant's provide no objective data in the instant specification. Examples A and B are directed to oral formulations comprising T3S. The paragraph spanning pages 9 and 10 states that "The pharmaceutical compositions of the present invention are usable in the treatment of pathologies due to organic deficiency of triiodothyronine **(T3),** like, for example, original hypothyroidism from autoimmune thyroid affections, hormonal production defects, thyroidectomy, congenital hypothyroidism, as well as some disorders due to reduced activity of type I 5'-iodothyronine monodeiodinase **(type** I **MD)** which is induced, for example, by hypothyroidism, non thyroidal systemic illnesses, fast, selenium shortage and so on." However, no objective data has been presented. Prophetic statements cannot take the place of objective data in showing that the invention is somehow non-obvious. In sum, applicant has not provided evidence of unexpected results to overcome the above *prima facie* case of obviousness.

Conclusion

Claims 9-15 and 25 are rejected. No claim is allowed.

No new ground(s) of rejection were presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kortney Klinkel, whose telephone number is (571)270-5239. The examiner can normally be reached on Monday-Friday 8am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached at (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

KLK

/Ashwin Mehta/
Primary Examiner, Art Unit 1638